REMARKS

Claims 1 – 21 are currently pending. Claims 1, 18, 19, and 21 are the pending independent claims. In the Office Action, Claims 1 – 17 and 21 were rejected under Section 112, first paragraph as allegedly failing to satisfy the written description requirement. On the merits, Claims 1-17 and 21 were rejected under 35 U.S.C. § 103(a) as allegedly obvious from U.S. Patent No. 4,929,605 to Domet et al. ("Domet") combined with U.S. Patent No. 4,176,175 to Maekawa et al. ("Maekawa"). Finally, Claims 18-20 were rejected as allegedly obvious over Domet in combination with U.S. Patent No. 6,380,381 to Obara et al. ("Obara").

Each of the foregoing rejections is respectfully traversed and favorable reconsideration is requested in view of the above amendments and following remarks.

I. The Written Description Rejections.

The Examiner contends that Claims 1 – 17 and 21 contravene the written description requirement of Section 112, first paragraph, alleging that the limitation "all of which are dispersed in the tablet core" constitutes new matter which is not disclosed in the specification. On the other hand, the Examiner acknowledges that the specification describes a composition in which the recited ingredients are "mixed into a tablet."

In response, Applicants have amended independent Claims 1 and 21 to delete the objected to "dispersed in the tablet core" language and to recite instead that the ingredients are incorporated into the tablet core as a part of a mixture.

In view of these amendments, it is submitted that all written description and other Section 112 rejections or objections are overcome and that the same should be withdrawn.

II. The Prior Art Rejections of Claims 1 – 17.

The Examiner continues to reject Claims 1-17 as allegedly obvious over Domet combined with Maekawa. Applicants urge the Examiner to reconsider and withdraw this rejection because it improperly attempts to combine features of disparate references that a person of ordinary skill would not be motivated to combine by any suggestion in the art in order to make Applicants' claimed composition.

Domet and Maekawa are not obviously combinable. One teaches specific tablet core compositions with no real concern about the composition of any coatings, while the other

teaches specific coating for formulations with no real concern about the internal composition of the tablets, etc. Nothing in one suggests any modification in the teachings of the other. One focuses on the outside. The other focuses on the inside. Nothing suggests trying to put them together in any way. But even if they were for some reason considered together, they would not contain what Applicants claim.

Neither of the cited references teaches a composition containing fexofenadine (in any form) intermixed with lactose and low-substituted HPC inside a tablet or particle core of a granulation or the like. Domet describes a highly specific strategy for attempting to improve the adsorption and bioavailability of piperidinoalkonal formulations (focusing on terfenadine) by including specific surfactants and carbonate salts together with certain "inerts." The focus of Maekawa is entirely different, dealing instead with specific sugar-coating layers of coatings said to speed up disintegration of the coatings in neutral or aqueous media. Maekawa is not particularly concerned with the composition of the interior or core. The alleged novel sugar-coating composition is said to be applicable to any solid dose core that might be amenable to a sugar coating. No descriptions are given of any solid dose composition ingredients, since that is not a focus of Maekawa .

Thus, as a threshold matter, Domet and Maekawa plainly do not present art teachings that would be "obviously" combinable for purposes of making a tablet or other particle core composition as claimed containing fexofenadine with improved bioavailability. One deals core compositions entered around the piperidinoalkanol terfenadine, while the other deal exclusively with sugar coatings applied to the outside of any compatible solid dose core composition.

In contrast to Domet and/or Maekawa, Independent Claim 1 of the present application (and therefore, by definition, each of its dependent claims) calls for, among other things, a pharmaceutical composition in the form of at least a tablet core which *consists essentially of a mixture of*: (1) *fexofenadine* or a pharmaceutical acceptable acid addition salt thereof, (2) about 10 wt. % to about 70 wt. % of *lactose*, and (3) about 1 wt. % to about 40 wt. % of a low-substituted hydroxypropyl cellulose.

Domet refers generally to piperidinoalkanol derivatives, and Domet only specifically mentions terfenadine. Nothing is said in Domet about fexofenadine in particular, nor does Domet purport to provide a specific core composition mixture that would allegedly improve the bioavailability of fexofenadine. For this reason, Domet plainly cannot be said to disclose much

less suggest any core composition of fexofenadine that includes lactose and L-HPC. Domet takes an entirely different approach in its effort to improve bioavailability of ternafadine by adding amionic/cationic surfactants plus carbonate salts.

Domet therefore cannot in fairness be said to suggest a tablet or other composition core which contains essentially only a mixture of lactose and L-HPC together with fexofenadine plus conventional excipients/inerts. The Examiner concedes this, but attempts to cure these deficiencies by reference to the Maekawa patent.

Once again, the Examiner's reliance on Maekawa is misplaced. Among other things, Maekawa only describes certain modifications of sugar-coatings. It cannot reasonably be said to suggest any modification to Domet's highly specific interior tablet core formulation.

Even if Maekawa dealt with the composition of a tablet or particle core, which it does not, the fact remains that it says nothing about lactose. While Maekawa makes a general reference to use of "sugar", the only sugar specifically taught in Maekawa is sucrose, and this is only in a coating. As the Examiner must know, sucrose is ordinary table sugar. Lactose is milk sugar. Consequently, one of skill following the teaching of Maekawa might have been lead to use "sucrose" in a sugar coating, but there is no objectively reasonable basis for someone of skill to choose "lactose" for use in a fexofenadine interior tablet core mixture from Maekawa's mention of sucrose in a sugar coating. Again, when a reference is cited in an obviousness rejection, the reference must be taken as a whole for all that it teaches, plus what it does not teach. *See In re Wesslau*, 353 F.2d 238, 241 (C.C.P.A. 1965).

If one of ordinary skill were to consider Domet and Maekawa in combination without any knowledge of Applicants' claimed formulation, and there is no objectively reasonable basis to suppose they would, nothing in these references would have lead a person of skill to prepare a tablet, granule, or particle core containing fexofenadine mixed with lactose and L-HPC as claimed.

In addition, Applicants note that they have amended the claims to clarify that the fexofenadine (or a pharmaceutical acceptable acid addition salt thereof) is provided as part of a mixture containing lactose and low-substituted hydroxypropyl cellulose in a tablet, particle, or granule core. This provides yet another start contrast between the subject matter of Applicants' claims and the teachings of Demot and Maekawa. The sucrose and low-substituted HPC disclosed in Maekawa are applied as part of an outer sugar-coating. Neither is included as an

essential part of a tablet or other core mixture containing fexofenadine as called for in the presently amended claims.

Finally, it is noted that Claim 1, and each of its dependent claims, is written in the partially closed "consisting essentially of" format. As the Examiner knows, this claim form is an accepted way for an applicant to convey its intention to exclude a reading of the claim that would encompass components in addition to fexofenadine, lactose, and a low-substituted hydroxypropyl cellulose (or other claimed materials/ingredients) which would "materially affect the basic and novel characteristics" of the claimed invention. *See Atlas Powder Co. v. E.I. du Pont de Memours & Co.*,750 F.2d 1569 (Fed. Cir. 1984). In this regard, it is noted that Domet specifically teach the inclusion of special types of surfactants and carbonate salts together with terfenadine as essential ingredients in the tablet core of their embodiments. The claim form used by Applicants does not mention surfactants or carbonate salts as being "essential." This provides still another objectively profound distinction between the subject matter of the present claims and the disparate disclosures of Domet and Maekawa relative to the claim scope being sought by Applicants.

In view of these and other manifest failings of Domet and Maekawa, it is respectfully submitted that there would be no objectively reasonable basis or motivation for a person of ordinary skill to attempt to combine the sugar coating formulations of Maekewa with the terfenadine tablet core compositions of Domet in the manner proposed by the Examiner (or in any other manner pertinent to Applicants' claimed invention) and, in any event, considering these references side-by-side would fail to suggest Applicants' pharmaceutical composition as defined in independent Claim 1 and its dependent claims, or in any of the other present claims. Thus, the obviousness rejections of these claims based upon Domet and Maekawa are not well founded and are contrary to law, and should be withdrawn.

III. The Prior Art Rejections of Claims 18 – 20.

Finally, the Examiner asserts that the subject matter of Claims 18-20 would have been obvious to a person of skill from a combination of Domet and Obara. It is respectfully submitted that these rejections are also unfounded and should be withdrawn.

Independent Claims 18 and 19 are each directed to a method for preparing a pharmaceutical composition which consists essentially of (1) fexofenadine or a pharmaceutical

acceptable acid addition salt thereof, (2) about 10 wt. % to about 70 wt. % of lactose, and (3) about 1 wt. % to about 40 wt. % of a low-substituted hydroxypropyl cellulose. In both claims, the first step is "mixing" the aforementioned fexofenadine, lactose, and low-substituted hydroxypropyl cellulose to form a premix. This is nowhere disclosed or even hinted at in Domet or Obara, either individually or in combination.

Like the rejection of the Claim 1 group, this rejection is built on an erroneous premise that a person of ordinary skill unaware of Applicants' invention would ignore the distinctly different orientations of two disparate references and still try to find some way to knit their teachings together. The narrow and different focus of Domet has already been explained, namely, a terfenadine tablet core containing particular surfactants and carbonate salts as essential ingredients for what are said to be better release properties once the tablets are imbibed. Obara is narrowly focused too, but in another and entirely different way. Obara's exclusive focus is on an alleged novel way to make low-substituted hydroxypropyl cellulose that beneficially affects its binding properties when used in processes that make pharmaceutical tablets by "wet granulation." In one of the examples, L-HPC is wet granulated with lactose. That's as close as Obara gets. No mention is made in Obara of the applicability of the process to the production of tablets containing any particular pharmaceutical. In fact, not a single active pharmaceutical is given in Obara.

So the gist of Obara is what is said to be, in essence, better L-HPC. But Applicants do not presume to have invented L-HPC, or a better method of making L-HPC. Applicants' claimed method simply uses L-HPC as one of the ingredients mixed with fexofenadine and lactose to make a premix that is then wet granulated and further processed as stated. Applicants' claimed method might, of course, be practiced with fexofenadine and lactose using any suitable L-HPC, and does not presuppose the existence or availability of any special new or improved L-HPC. Nothing about Obara's disclosure of a way to make allegedly better L-HPC would have led a person of skill to modify Domet to make a fexofenadine pharmaceutical tablet core by premixing fexofenadine with lactose and L-HPC as called for in Claims 18 -20.

Further, as the Examiner concedes, Domet fails to suggest the use of lactose and a low-substituted hydroxypropyl cellulose in his tablet.

Further, as mentioned above, Domet specifically teaches the inclusion of a surfactant as an essential ingredient together with the active ingredient terfenadine. This is contrary to what

is called for in Claims 18 and 19, which are directed to a method for making a pharmaceutical composition which includes the step of making a premix that consists essentially of a mixture of (1) fexofenadine or a pharmaceutical acceptable acid addition salt thereof, (2) lactose, and (3) a hydroxypropyl cellulose. Surfactant is not an "essential" ingredient in Applicants' claimed method.

Accordingly, there is no objectively reasonable basis or incentive for a person of ordinary skill in the art to have modified the teachings of Domet based upon the disclosure of Obara in an effort to make a pharmaceutical composition according to Applicants' claims. Again, Applicants' Claims 18-20 do not purport to rely upon any alleged new or improved L-HPC, nor is there any objectively rational basis to suppose the isolated teaching in Obara of an alleged better L-HPC would somehow spark a person of ordinary skill to change Domet's method (which, incidentally, does not even use L-HPC) so as to produce fexofenadine tablet (or other compositional) cores by a process including wet granulation of a mixture that include at least fexafenadine, lactose, and L-HPC as the essential ingredients. Such a result could only conceivably result from either some serendipitous circumstance or other "inventive" activity or a process of hindsight reconstruction of the claimed process from a foreknowledge of Applicants' invention. But it cannot reasonably be said to result from any "obvious" conclusion or discernment from consideration of these otherwise disparate references.

In light of the foregoing, the present amendment is believed to place the application in a condition for allowance and entry of the foregoing amendments and allowance of Claims 1 – 21 is respectfully solicited.

In the event this response is not timely filed, Applicants hereby petition for the appropriate extension of time and request that the fee for the extension along with any other fees which may be due with respect to this paper be charged to our Deposit Account No. 12-2355.

Respectfully submitted,

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January 30, 2009

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